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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/183,055	10/29/98	JUNE C	RPI-002CPBCN

HM12/1120

LAHIVE & COCKFIELD
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EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	11

DATE MAILED: 11/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

UNITED STATES DEPARTMENT OF COMMERCE
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 6/30/00; 9/15/00

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1, 46, 47, 50-58, 69-72 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 1, 46, 47, 50-58, 69-72 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☑ Notice of Reference Cited, PTO-892 ☑ NOTICE TO COMPLY WITH SEQUENCE RULES
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

1. Applicant's amendment, filed 9/15/00 (Paper No. 10), is acknowledged.
Claims 45, 48, 49 and 59-68 have been canceled. Claims 2-44 have been canceled previously.
Claims 1, 46, 47, have been amended.
Claims 71 and 72 have been added.

Claims 1, 46, 47, 50-58 and 69-72 are pending.

Applicant's election of Group II with traverse in Paper No. 9, filed 6/30/00, is acknowledged.

However, given applicant's pending claims, the previous restriction requirement is rendered moot. Therefore, claims 1, 46, 47, 50-58 and 69-72 are under consideration in the instant application.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the CRF submission filed 10/12/99 fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The following procedure is to be used for cases that contain the same sequence disclosure as the parent. The applicant need not submit a new computer readable from of the Sequence Listing in this continuation. However, (1) the specification must contain a paper copy of the Sequence Listing, (2) applicant must request in writing that the CRF in the parent case be used to prepare a file for the offspring and (3) applicant must submit a statement that the paper copy of the Sequence Listing in the offspring is identical to the computer readable form submitted in the parent case.

Applicant is reminded to amend the specification and the claims accordingly, if necessary.

3. The drawings submitted with this application were declared informal by the applicant. Accordingly, they have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review

The Brief Description of the Drawings should be amended to recite the different part numbers of the drawings (e.g. Figures 5A-C).

4. Applicant is reminded to amend the first line of the specification to update the status of priority documents

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

6. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

7. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected. In addition, applicant should carefully review the application for other errors such as missing information (see page 35, line 7).

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant should carefully remove the specification for corrections

8. The instant methods do not receive priority back to USSN 07/275,433, filed 11/23/88, because USSN 07/275,433 does not appear to provide written support for "methods for including $CD8^+$ T cells within a population of T cells, comprising activating a population of T cells by contacting said population of T cells with an anti-CD3 antibody and stimulating an accessory molecule on the surface of the T cells with a ligand which binds the accessory molecule, the activating and stimulating steps thereby inducing proliferation of $CD8^+$T cells ".

If applicant desires priority back to USSN 07/275,433, filed 11/23/88; applicant is invited to point out and provide documentary support for the priority of the instant claims. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Given the number of continuation-in-part priority applications, applicant is invited to indicate the particular priority application, upon which applicant is relying upon for earliest priority of the claimed invention / "limitations".

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 46, 47, 50, 51, 52 and 71 are rejected under 35 U.S.C. § 102(b) as being anticipated by Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #D7) (see entire document; including Abstract, Results and Discussion). Weiss et al. teach stimulating proliferation in enriched T cells which comprise CD8+ T cells with immobilized anti-CD3 antibodies and anti-Tp44 antibodies (i.e. anti-CD28). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods.

12. Claims 1, 46, 47, 50, 51, 52 and 71 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B13) (see entire document; including Abstract, Results and Discussion). Ledbetter et al. teach augmenting and sustaining the proliferation in mononuclear cell populations which comprise CD8+ T cells with immobilized anti-CD3 antibodies and anti-Tp44 antibodies (i.e. anti-CD28). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods.

13. Claims 1, 46, 47, 50, 51, 52, 56 and 71 are rejected under 35 U.S.C. § 102(b) as being anticipated by Thompson et al. (WO 90/05541) (1449, #A3) (see entire document). Thompson et al. teach methods of immunotherapy by stimulating T cells with immobilized anti-CD3 antibodies and anti-CD28 (see Examples III-VIII). Also, Thompson et al. teaches such methods are desirable for enhancing T cell immune responses directed specifically towards T cells activated by antigen (page 1-2, overlapping paragraph). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods.

14. Claims 1, 46, 47, 50, 51, 52, 56-58 and 71 are rejected under 35 U.S.C. § 103 as being unpatentable over Zarling et al. (U.S. Patent No. 5,081,029) in view of Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #D7) AND/OR Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B13).

Zarling et al. teaches methods of adoptive immunotherapy for treating various disorders, including stimulating antigen-specific T cells comprising $CD3^{+}CD^{+}$ T cells, including the use various stimuli including anti-Tp44 antibodies (column 7, paragraphs 1-2) for the expansion of t cells for adoptive immunotherapy(see entire document, including Summary of the Invention, Detailed Description of the Invention, Isolation, Activation and Expansion of Lymphocytes, including Examples).

Zarling et al. differs from the claimed methods by not disclosing the art known use of immobilized anti-CD3 antibodies in the stimulation of T cells of interest at the time the invention was made.

Weiss et al. teach stimulating proliferation in enriched T cells which comprise CD8+ T cells with immobilized anti-CD3 antibodies and anti-Tp44 antibodies (i.e. anti-CD28) (see entire document; including Abstract, Results and Discussion)

Ledbetter et al. teach augmenting and sustaining the proliferation in mononuclear cell populations which comprise CD8+ T cells with immobilized anti-CD3 antibodies and anti-Tp44 antibodies (i.e. anti-CD28) (see entire document; including Abstract, Results and Discussion).

Given the art known use of applying immobilized anti-CD3 antibodies and anti-Tp44 (i.e. anti-CD28) antibodies to stimulate T cells, as taught by the combined teachings of Zarling et al., Weiss et al. And Ledbetter et al.; one of ordinary skill in the art would have been motivated to stimulate antigen-specific T cells in large numbers, needed for adoptive immunotherapy to antigens of interest. Therefore, one of ordinary art at the time the invention was made would have expected to monitor the proliferation of said antigen-specific T cells , to re-stimulate T cells undergoing expansion to achieve large number of cells (e.g. 100-100,000-fold) required for adoptive immunotherapy.

One of ordinary skill in the art at the time the invention was made would have been motivated to stimulate T cell activation with both CD3-/CD28-specific antibodies to increase T cell proliferation and numbers of T cells of interest for various purposes, such as T cell studies and adoptive immunotherapy. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

14. Claims 1, 46, 47, 50, 51, 52, 56-58 and 71 are rejected under 35 U.S.C. § 103 as being unpatentable Thompson et al. (WO 90/05541) (1449, #A3) (see entire document).

Thompson et al. teach methods of immunotherapy by stimulating T cells with immobilized anti-CD3 antibodies and anti-CD28 (see Examples III-VIII). Also, Thompson et al. teaches such methods are desirable for enhancing T cell immune responses directed specifically towards T cells activated by antigen (page 1-2, overlapping paragraph).

Thompson et al. differs from the claimed methods by not explicitly teaching the monitoring of stimulated T cell populations comprising CD8+ T cells and the percent increases in T cell populations encompassed by the claimed invention.

Given the art known use of applying immobilized anti-CD3 antibodies and anti-Tp44 (i.e. anti-CD28) antibodies to stimulate T cells, as taught by Thompson et al.; one of ordinary skill in the art would have been motivated to stimulate antigen-specific T cells in large numbers, needed for adoptive immunotherapy to antigens of interest, also as taught by Thompson et al.. Therefore, one of ordinary art at the time the invention was made would have expected to monitor the proliferation of said antigen-specific T cells , to re-stimulate T cells undergoing expansion to achieve large number of cells (e.g. 100-100,000-fold) required for adoptive immunotherapy.

One of ordinary skill in the art at the time the invention was made would have been motivated to stimulate T cell activation with both CD3-/CD28-specific antibodies to increase T cell proliferation and numbers of T cells of interest for various purposes, such as T cell studies and adoptive immunotherapy. From the teachings of the reference, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

15. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

16. Claims 1, 54, 55, 69 and 72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23, 25-33 of U.S. Patent No. 5,858,358 (June et al.) in view of Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #D7) AND/OR Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B13) (as they read on methods employing anti-CD9, anti-CD3 and anti-CD28 antibodies to stimulate T cells, including $CD8^+$ T cells).

Although the conflicting claims are not identical, the are not patentably distinct from each other because the instant claims, as they read on stimulating the proliferation of T cells, including CD8+ T cells, appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of CD9-specific antibodies, including the ES5.2D8/SEQ ID NO: 5 specificities of the patented methods. Although the patented methods recite the CD3 specificity and do not recite the CD28 specificity per se; stimulating T cell populations with anti-CD3 and anti-CD28 antibodies were known and obvious at the time the invention was made, as taught by Weiss et al and Ledbetter et al. above. In addition, the use of the other patented stimulating agents such as calcium ionophore and protein kinase C activators were known and practiced as T cell activators in stimulating T cell populations, including $CD8^+$ T cells at the time the invention was made.

17. Claims 1, 54, 55, 69 and 72 are directed to an invention not patentably distinct from claims 1-23, 25-33 of commonly assigned U.S. Patent No. 5,858,358 (June et al.)) in view of Weiss et al. (J. Immunol. 137: 819-825, 1986; 1449, #D7) AND/OR Ledbetter et al. (J. Immunol. 135: 2331-2336, 1985; 1449, #B13) for the reasons above in Section 16 (as they read on methods employing anti-CD9, anti-CD3 and anti-CD28 antibodies to stimulate T cells, including $CD8^+$ T cells).

Commonly assigned June et al. (U.S. Patent No. 5,858,358); discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

18. Claims 1, 46, 47, 50, 51, 52, 56-58 and 71 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims (52, 62, 65, 80, 81, 84, 86, 88, 90, 92, 94, 95, 98, 99 and 102) of copending USSN 08/403,253 and claims (50-55, 57 and 59) of copending USSN 09/350,202;
(as they read on methods employing anti-CD3 and anti-CD28 antibodies to stimulate T cells, including $CD8^+$ T cells; excluding anti-CD9 antibodies)

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant and copending claims appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of anti-CD3 and anti-CD28 antibodies to stimulate and expand T cells, including CD8+ T cells.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Claims 1, 46, 47, 50, 51, 52, 56-58 and 71 are directed to an invention not patentably distinct from claims (52, 62, 65, 80, 81, 84, 86, 88, 90, 92, 94, 95, 98, 99 and 102) of commonly assigned copending USSN 08/403,253 and
claims (50-55, 57 and 59) of commonly assigned copending USSN 09/350,202;
(as they read on methods employing anti-CD3 and anti-CD28 antibodies to stimulate T cells, including $CD8^+$ T cells; excluding anti-CD9 antibodies) for the reasons set forth above in Section 18.

Commonly assigned USSN 08/403,253 and USSN 09/350,202; discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

20. No claim is allowed.

Claims 1, 54, 55, 69 and 72 as they read on methods employing anti-CD9, anti-CD3 and anti-CD28 antibodies to stimulate T cells, including $CD8^+$ T cells appear to be free of the prior art, other than the obvious double patenting rejection set forth herein.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
November 20, 2000